Remarks

Claims 1-5 were previously pending in this application.

Applicant has amended claim 1 and added new claims 39-58. Upon amendment, claims 1-5 and 39-58 are currently pending for examination with claims 1 and 51 being the independent claims. The amendment of claim 1 and new claims 39-58 are supported by the specification and claims as originally filed. More particularly, the amendment of claim 1 and new claims 39-50 are supported in the specification at, e.g., page 7, lines 12-29 and 32, and page 9, lines 1-2. New claims 51-54 are supported in the specification at, e.g., page 7, lines 26-29, and page 16, lines 25-32. New claims 55-58 are supported, e.g., by original claims 2-5. No new matter has been added.

Rejections under 35 U.S.C. §112, First Paragraph – Written Description

The Examiner rejected claims 1-5 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. *See* the OA, page 2. In particular, the Examiner pointed out that "the claims broadly encompass a genus of Akt molecules; [h]owever, the written description in this case only sets forth one species of an Akt molecule represented by SEQ ID NO:1 and 2." *Id.*, page 3.

For reasons set forth below, Applicant respectfully disagrees. Briefly, Applicant respectfully submits the written description in this case sets forth considerably more than one species of an Akt molecule represented by SEQ ID NO:1 and 2. However, for the sole purpose of advancing prosecution, Applicant has amended claim 1 and added new claims 39-58 to make clear that the pending claims are in fact directed to a method for treating myocardial infarction using an Akt molecule, wherein said Akt molecule is either an *Akt nucleic acid* or an *Akt polypeptide*. *See* page 7, lines 26-27 et seq.

As the Examiner noted, Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555 (Fed. Cir. 1991), sets forth the standard of the written description requirement under 35 U.S.C. § 112, first paragraph. *See* the OA, page 3. "If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, ... then the adequate description requirement is met." Vas-Cath, at 1563. When a claim is drawn to a genus, the written description

requirement can be satisfied by sufficiently describing a representative number of species by actual reduction to practice, or by disclosure of relevant identifying characteristics sufficient to show the applicant was in possession of the claimed genus. *See* MPEP 2163; *see also* University of California v. Eli Lilly, 119 F.3d 1559, at 1568 (Fed. Cir. 1997).

The pending claims in the instant application cover a method for treating myocardial infarction by administering to a subject in need either an Akt nucleic acid or an Akt polypeptide. As is apparent from the specification and the discussion below, the Akt nucleic acid can comprise or consist of a nucleic acid sequence encoding an Akt polypeptide which shares at least 98% amino acid identity with SEQ ID NO:2.

Claims 1 and 51 encompass a genus of Akt nucleic acids and a genus of Akt polypeptides, respectively. At a minimum, the specification discloses both human and mouse Akt molecules, including both nucleotide sequences (SEQ ID NOs 1, 3, and 5) and amino acid sequences (SEQ ID NOs 2, 4, and 6). *See* page 7, lines 12-18. SEQ ID NO:1 is disclosed as a preferred Akt nucleic acid at page 8, line 3.

In claim 1, the Akt nucleic acid is limited to the polypeptide it encodes. On page 7 of the specification it is disclosed that

> *Although use of the mouse Akt compositions is exemplified in the Examples section, it is believed that the results obtained using such compositions are predictive of the results that may be obtained using the human sequences, since the mouse c-akt is 90% homologous to human Akt at the nucleic acid level and 98% homologous at the amino acid level.*

In fact, comparison of SEQ ID NO:2 (human Akt) and SEQ ID NO:6 (mouse Akt) reveals 98% *identity* at the amino acid level. Furthermore, comparison of SEQ ID NO:4 (N-terminal truncated form of human Akt) with corresponding sequence of SEQ ID NO:2 reveals 98% *identity* at the amino acid level.

Since the genetic code is widely known, disclosure of an amino acid sequence would provide sufficient information such that an artisan in the pertinent art would recognize that Applicant was in full possession of the claimed genus of nucleic acids encoding the claimed Akt

polypeptide. *See* In re Bell, 991 F.2d 781; *see also* MPEP 2163. Therefore, a person skilled in the art would have understood that Applicant was in full possession of the claimed genus of Akt nucleic acids recited in claim 1, without the disclosure of each and every species thereof.

The Akt polypeptide recited in claims 1 and 51 is specified as sharing at least 98% amino acid identity with a defined amino acid sequence (SEQ ID NO:2). Since the amino acid sequence is a prominent characteristic of a polypeptide, the disclosure of the instant application is sufficient to show a person skilled in the art that Applicant was in possession of the Akt polypeptide recited in the claims.

In addition, the instant application teaches the use of both an Akt nucleic acid and an Akt polypeptide as described above to treat myocardial infarction by inhibiting cardiac tissue necrosis. *See* page 7, lines 1-8. In particular, it provides an example of using mouse Akt to protect against myocyte apoptosis in response to ischemia-reperfusion injury. *See* page 48-54, Example 4. Taken together, Applicant has provided sufficient written description to show a person skilled in the art that Applicant was in possession of the claimed method for treating myocardial infarction by using an Akt nucleic acid or an Akt polypeptide as of the filing date of this application.

The Examiner cited Fiddes v. Baird, 30 USPQ2d 1481, to support his rejection of claims 1-5 for alleged lack of sufficient written description. However, the Fiddes case is factually distinguishable from the instant application. In Fiddes, the claims broadly encompassed DNA sequences encoding mammalian basic FGF, while the written description only disclosed the amino acid sequence of a single, particular FGF, bovine FGF. The applicant neither disclosed the natural DNA sequence encoding the bovine FGF, nor did he disclose any naturally-occurring nucleotide sequences encoding any mammalian FGF. Accordingly, the court held that the patent application failed to provide a sufficient description "since knowledge of amino acid sequence of a protein, coupled with established relationship in genetic code between nucleic acid and protein it encodes, would not establish inventor's possession of gene encoding that protein." *Id.*, at 1483.

In contrast, the specification in this application not only discloses amino acid sequences of both human and mouse Akt polypeptides, but also corresponding natural DNA sequences

encoding these Akt polypeptides. Further, the specification teaches that the mouse Akt is structurally highly homologous and functionally equivalent to its human counterpart. *See* page 17, lines 21-24. Therefore, the disclosure of the instant application is sufficient to establish Applicant's possession of both the genus of Akt nucleic acids and the genus of Akt polypeptides as recited in the pending claims. Accordingly, Applicant respectfully submits that reliance on Fiddes is misplaced in this case.

In view of the foregoing, Applicant respectfully requests withdrawal of the rejections of claims 1-5 under 35 U.S.C. §112, first paragraph, for allegedly failing to satisfy the written description requirement.

Rejections Under 35 U.S.C. §112, First Paragraph – Enablement

The Examiner rejected claims 1-5 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the enablement requirement. In particular, the Examiner pointed out that "[t]he claims are broadly drawn to a method of treating myocardial infarction comprising administering to a subject in need of such treatment an Akt molecule in an amount effective to inhibit cardiac tissue necrosis." *See* the OA, page 5. The Examiner further pointed out that "[a] method of treating a subject for myocardial infarction, comprising the step of: administering to the subject in need of such treatment a composition comprising a replication-defective adenovirus comprising a polynucleotide, wherein said composition is administered acutely into the apical and anterolateral free wall of the heart, wherein said polynucleotide comprises a nucleotide sequence that encodes an Akt polypeptide, operatively linked to a promoter to promote expression of the Akt polypeptide in cardiomyocytes, wherein the Akt polypeptide comprises the amino acid sequence of SEQ ID NO:2-- does not reasonably provide enablement for the broadly claimed invention." *See* the OA, pgs 4-5.

The enablement requirement is satisfied when the application provides sufficient information to enable a person skilled in the pertinent art to make and use the claimed invention commensurate in scope with the claims. *See* MPEP 2164.01 and 2164.07. The specification need not necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of prior art and routine experimentation can often fill gaps

interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments. *See* Chiron Corp. v. Genetech, Inc., 363 F.3d 1247.

As noted above, the pending claims are directed to a method for treating myocardial infarction by using either an Akt nucleic acid or an Akt polypeptide as recited in claim 1 and claim 51, respectively. In view of the disclosure of both a nucleotide sequence and an amino acid sequence of the human Akt (e.g., SEQ ID NO:1 and NO:2, respectively), a person skilled in the art would know how to make and use a nucleic acid encoding a polypeptide that shares at least 98% amino acid identity with the defined amino acid sequence. He would also know how to make and use a polypeptide that shares at least 98% amino acid identity with SEQ ID NO:2.

Further, the specification teaches that Akt is a serine-threonine kinase and can phosphorylate proteins involved in apoptotic cell death, such as *Bad*, resulting in the inactivation of these proteins and cell survival. *See* page 2, lines 9-13. Based on the biological function of Akt, the instant application further teaches that either an Akt polypeptide, or an Akt nucleic acid that encodes an Akt polypeptide in cells, can be used to inhibit apoptotic cell-death, in particular, to treat conditions such as myocardial infarction. *See* page 2, lines 16-20. Specifically, it teaches that Akt protected against myocyte apoptosis in response to ischemia-reperfusion injury following its transduction into a mouse heart. *See* page 48, lines 30-32.

It is well known in the art that proteins, which are highly homologous at the amino acid level, e.g., sharing >95% amino acid identity, are very likely to have the same biological function. In this case, the specification teaches that mouse Akt is 90% homologous to human Akt at the nucleic acid level and 98% homologous (indeed, 98% identical) at the amino acid level. *See* page 7, lines 21-22. Further, the specification teaches that both mouse Akt and human Akt may have the same effect of protecting against myocyte apoptosis in response to ischemia-reperfusion injury. *See* page 17, lines 21-24. Thus, it is predictable that an Akt polypeptide as recited in pending claims would have the same biological function as human Akt, e.g., being a serine-threonine kinase and capable of inhibiting apoptotic cell-death. It is also predictable that an Akt nucleic acid encoding an Akt polypeptide as recited in pending claims can be used to treat myocardial infarction in a subject in need.

It appears that the Examiner may have misinterpreted the claimed invention. The Examiner's interpretation of the claimed invention as noted above represents just a preferred embodiment of the invention, but not the claimed invention as a whole.

First, the claimed method is not limited to the use of "*a composition comprising a replication-defective adenovirus comprising a polynucleotide.*" *See* the OA, pgs 4-5. The specification teaches that both an Akt nucleic acid and an Akt polypeptide can be used in the method of treating myocardial infarction. *See* page 2, lines 16-22 and lines 31-32. Since an Akt polypeptide is the ultimate factor having the therapeutic effect, direct administration of an Akt polypeptide would have the same effect as administration of a DNA construct capable of directing expression of an Akt polypeptide. Therefore, a person skilled in the art would recognize that the instant application encompasses the use of both an Akt nucleic acid and an Akt polypeptide in the claimed method.

Second, the claimed method is also not limited to "*acute administration into the apical and anterolateral free wall of the heart.*" *See* the OA, page 5. A person skilled in the art would know that any method available in the prior art to deliver either nucleic acids or polypeptides to a tissue would also be applicable in the claimed invention. The specification also teaches that "preferred methods of administration ... include direct intramuscular injection into the myocardium, catheterization of the heart, and intraarterial administration." *See* page 19, lines 25-28.

Finally, the Examiner stated that "although the specification teaches the adenoviral vectors were used in the delivery, the claims are not limited to any specific delivery protocol, vector system or delivery locale." *See* the OA, page 6. Again, using the adenovirus delivery system is disclosed as one preferred embodiment of the claimed invention. The specification teaches that an Akt molecule (including both an Akt nucleic acid and an Akt polypeptide) can be delivered in association with a vector, which is a vehicle capable of facilitating the delivery of an Akt molecule to a target cell and/or uptake of an Akt molecule by a target cell. *See* page 10, lines 30-33 and page 11, line 11. A nucleic acid vector is disclosed to include, *inter alia*, plasmids, phagemids, viruses, etc. *See* page 11, lines 12-21. The specification also teaches that an Akt molecule can be delivered by, for example, a colloidal dispersion system, *see* page 13, lines 12-24, a liposome, *see* page 13, lines 25-30, or a biocompatible micro particle or implant,

see page 14, lines 8-30. Taken together, the claimed invention disclosed in the instant application has a much broader scope than that of the Examiner's interpretation.

Pursuant to Chiron, it is unnecessary that the instant application should teach how to make and use each and every Akt species to treat myocardial infarction. As discussed above, it is within the abilities of a person skilled in the art how to make and use the Akt nucleic acid and the Akt polypeptide as claimed in claim 1 and claim 51. The knowledge of a person skilled in the art and routine experimentation also can fill the gap of delivering every species of the Akt (nucleic acid and polypeptide) into a subject to treat myocardial infarction. To summarize thus far, Applicant respectfully submits that the specification provides sufficient direction to satisfy the enablement requirement under 35 U.S.C. § 112, first paragraph.

The Examiner further rejected claims 1-5 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement on the ground that gene therapy is unpredictable. Citing two references ("Crystal" and "Anderson"), the Examiner asserted that the lack of safe and efficient gene-delivery system rendered the technology of gene therapy unpredictable. *See* the OA, page 6.

It must be noted that neither Crystal nor Anderson denies the effect of transferring genes into human body and then evoking expected biological responses. *See*, e.g., Crystal, page 405, right column ("Probably the most remarkable conclusion drawn from the human trials is that human gene transfer is indeed feasible."); *see also Id.*, page 408, left column ("Experience with marking studies has shown that human gene transfer can yield important insights into human biology by making it possible to track the fate of genetically marked cells in a recipient.").

While both Crystal and Anderson point out that a challenge of gene therapy is the development of "safe and efficient gene-delivery systems," *see*, e.g., Crystal, page 409 and Anderson, page 25, safety and efficiency are not the relevant standard for enablement under 35 U.S.C. § 112, first paragraph. MPEP 2164.01(c) makes it clear that "the applicant need not demonstrate that the invention is completely safe." In fact, it is within the domain of concern of the Food and Drug Administration, but not that of the Patent Office, to determine whether a pharmaceutical composition or treatment is safe and effective when applied in human clinical use. In other words, matters of safety and efficiency, being outside the enablement standard as

the law requires, thus should not pose a bar to patentability. *See* In re Brana, 51 F.3d 1560 (Fed. Cir. 1995).

In view of the foregoing, Applicant respectfully requests withdrawal of the rejections of claims 1-5 under 35 U.S.C. §112, first paragraph, for allegedly failing to satisfy the enablement requirement.

Conclusion

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
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